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How does PET/MR work? Basic physics for physicians

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Abstract

The aim of this article is to provide Radiologists and Nuclear Medicine physicians the basic information required to understand how PET/MR scanners work, what are their limitations and how to evaluate their performance. It will cover the operational principles of standalone PET and MR imaging, as well as the technical challenges of creating a hybrid system and how they have been solved in the now commercially available scanners. Guidelines will be provided to interpret the main performance figures of hybrid PET/MR systems.

Key words: Simultaneous PET/MR—Time-of-flight PET—Attenuation correction—Magnetic resonance imaging—Positron emission tomography

Thirteen years after its commercial introduction, integrated positron emission (PET) and computed tomography (CT) have evolved into one of the major imaging procedures in oncology, infection imaging, and cardiology. However, PET/CT has several limitations, both technical and diagnostic, that have recently led to the emergence of hybrid PET and magnetic resonance (MR) scanners [1–3]. Among other advantages, PET/MR imaging offers superior soft tissue contrast (e.g., higher sensitivity for small liver metastasis, additional information for lesion characterization, better depiction of pelvic structures) and lower radiation exposure to the patient.

The aim of this article is to provide Radiologists and Nuclear Medicine physicians the basic information required to understand how PET/MR scanners work, what are their limitations, and how to evaluate their performance.

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How does PET work?

PET is a Nuclear Medicine imaging technique developed in the 1950s and adapted for clinical practice in the 1970s [4, 5]. As with other Nuclear Medicine techniques, PET is based on administering targeted drugs labeled with a radioactive isotope. By detecting the emitted radiation, the biodistribution of the drug can then be inferred.

The brilliant idea behind PET is to use positron-emitting isotopes. Positrons are elementary particles, the antimatter counterpart of electrons. When a positron is emitted by a radioactive isotope, it will typically travel a few millimeters before colliding with one of the electrons in the surrounding tissue. The two particles will then annihilate, (typically) emitting two photons in (quasi) opposite directions (Fig. 1). The beauty of this is that, if we are somehow capable of detecting both photons, we will then know for a fact that the annihilation occurred somewhere along the line between both detections. That makes it a very similar problem to that of transmission imaging (e.g., X-ray CT) and one that we know well how to solve.

How do we go about detecting those high-energy annihilation photons, when two inches of concrete would not suffice to stop half of them? The detectors most commonly found in state-of-the art PET and PET/CT scanners use a two-step approach: First, several centimeters of a high-density scintillator material are used to convert the annihilation photon into multiple lower energy photons. These are then collected by a photomultiplier tube (PMT), a type of electronic light sensor coupled to the scintillator.

Dedicated circuitry analyzes the output of the photomultiplier to determine the energy and precise timing of the detected photon. The former is used to reject photons that have been deflected (scattered) from their original path, due to Compton interactions with either patient tissue or hardware placed in the field of view (e.g., MR coils). The latter is critical to determine whether a

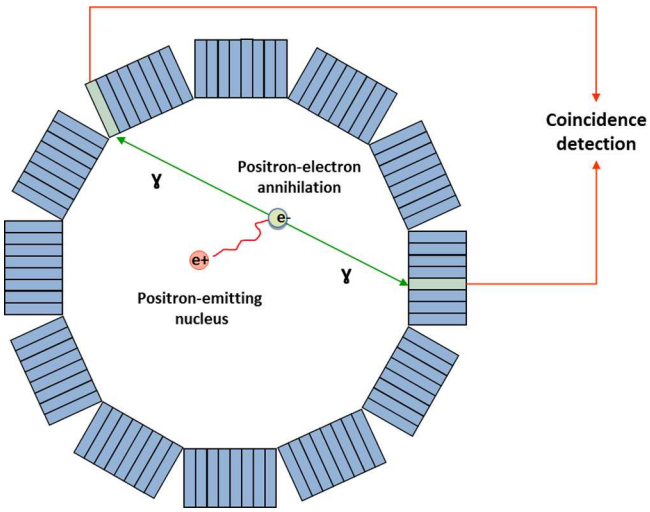

Fig. 1. Schematic representation (transaxial view) of the PET imaging principles: A positron is emitted during the disintegration of a radioactive isotope. This positron typically travels for a few millimeters before annihilating with an electron of the surrounding tissue. Two annihilation photons are emitted in (approximately) opposite directions. When both photons interact with the scintillator crystals of the PET detector ring, a coincidence event is recorded.

second, matching annihilation photon has been registered by one of the other detectors. Furthermore, good enough timing accuracy can be used to narrow down the region where the annihilation occurred (this is known as Time-of-Flight information, or ToF). As a reference, a PET detector with a timing resolution of 500 ps will be able to place the position of annihilation within a 7.5 cm region, whereas a future system with 100 ps resolution would reduce that to a 1.5 cm region, thus making image reconstruction considerably easier.

Despite the obvious challenges of intercepting and sorting high-energy photons, it is important to contemplate the scale at which we are working: Given enough time, each molecule of radiotracer will emit some radiation. Typically, a state-of-the-art scanner will capture around 1% of that. In other words, all it takes is a few hundreds of molecules at a given location to get a blip in our radar. It is of course a very optimistic oversimplification but, still, this kind of sensitivity is orders of magnitude away from what other modalities can ever achieve. Together with the flexibility in the design of custom radiotracers to target new metabolic parameters, these are the main strengths of PET.

How does MR work?

Magnetic resonance imaging (MRI) is a medical imaging technique that, similarly to PET, was already postulated in the 1950s [6] but had to wait until the late 1970s to be adapted for clinical practice [7]. In MRI, the patient is placed in a strong constant magnetic field. Certain particles within the patient body (such as the abundant hydrogen nuclei) will tend align with this field. Think of it like tensing the strings of a guitar: Particles (our strings) have now a clear preferred state. When forced out of this state (plucked) they will try to get back to it, each following a different pattern that tells about its composition and surroundings.

So, how do we pull a particle's magnetic moment away from its preferred state of alignment? Surely not with a second, huge, outrageously expensive magnet? Fortunately not. It turns out that a well-timed (resonant) electromagnetic wave can do the trick. The kind of wave that can be generated with little more than a wire loop of the right shape. The physics behind this effect are called *Larmor precession* and dictate which will be the precise frequency at which the magnetic moments will resonate, given an external magnetic field (known as the *Larmor frequency*).

Notice that this approach would yield the response of all particles simultaneously, good enough for some applications (like the spectroscopic analysis of a small sample) but definitely not enough for imaging. In order to discern the origin of each signal, additional hardware is introduced that slightly alters the main magnetic field, gradually changing its strength throughout the field of view. As the Larmor precession frequency is proportional to the external magnetic field, different regions in the image will now emit slightly different frequencies, as well as slowly de-phase. Both these effects can be exploited to sort the received signals in space, creating reconstructed MRI images as we know them.

The typical configuration of a clinical whole-body scanner is a concentric arrangement of cylindrical coils (Fig. 2): A large superconducting coil to maintain the

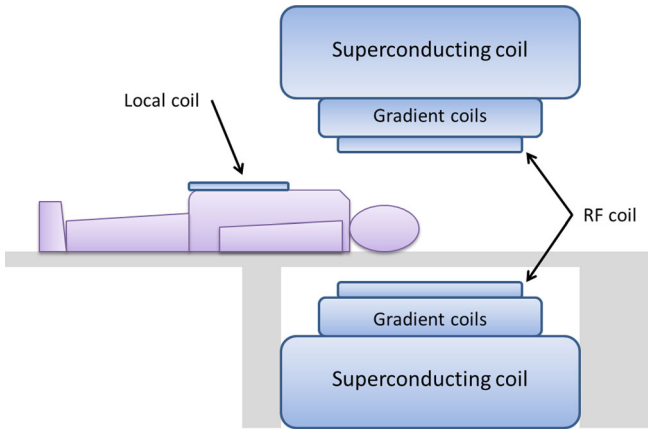

Fig. 2. Schematic representation (sagittal view) of an MR scanner. The permanent superconducting coil, gradient *x*–*y*–*z* coils, and radiofrequency transmit/receive coil are arranged as concentric cylinders, leaving a 60–70 cm bore for the patient bed to slide in. Local radiofrequency coils can be placed directly on the patient for improved signal quality.

static field (roughly 7000 kg and 1.5–2.0 mm long, with ~90 cm bore diameter), a set of three gradient coils for spatial encoding (~90 cm outer and ~65 cm inner bore diameter) and a transmit–receive radiofrequency coil (~60 cm bore diameter). Optionally, transmit and/or receive can be achieved by movable coils designed for specific locations (head, knee, endorectal, etc.) This allows a more specific delivery of the radiofrequency and better signal reception.

Combining PET and MR: challenges

In contrast to the relatively straightforward development of PET/CT scanners, the combination of MR and PET has proven to be very challenging. The intense static field, the quickly changing gradient fields, and the radiofrequency pulses, all required for MR imaging, prevent the normal operation of PET detectors (especially those based on PMT technology). Conversely, the mere presence of the PET detector degrades the performance of each of those MRI components. We summarize in the following paragraphs the main physical incompatibilities between PET and MR.

MRI relies on the assumption that the static field is perfectly uniform. Inhomogeneities in this field can lead to artifacts in the reconstructed images. Unfortunately, materials placed in a magnetic field (such as a bunch of PET detectors) become magnetized, disturbing the uniformity of the field.

Also, a magnetic field will deflect charged particles moving through it. Which has a crippling effect in the PMTs used in standard PET detectors [8].

Time-varying magnetic fields (such as the gradient fields used for spatial encoding) induce unwanted currents in conductive structures (such as the PET detector circuitry). These local current loops, known as eddy currents, degrade the performance of the gradients and the homogeneity of the static field. They can cause distortions in the reconstructed images and signal loss.

Furthermore, eddy currents will cause heating, which throws off the delicate calibration of the PET detectors [9–11]. Worse, it does so in time-varying, hard to predict patterns that depend on the particular MR sequences being acquired.

Electronic cross-talk is another potential source of performance degradation and artifacts. On the one hand, the strong signals emitted by MR can induce currents directly in the PET detector electronics (causing, for example, fake detection events). On the other hand, PET detectors emit unwanted signals that, albeit weak, can be picked up by the sensitive MR reception (MR signals are extremely weak themselves, requiring very high-gain receivers). Keep in mind that the magnetic resonance signal is extremely weak and can be contaminated by the slightest perturbance. This is the reason why MR systems must operate within a Faraday cage.

Finally, an important factor affecting the quality of PET images is the attenuation caused the different elements in the field of view (mostly the patient, but also scanner hardware such as local MR coils). The annihilation photons have a probability of interacting with any materials along their path, becoming scattered away from their original trajectory and, in most cases, lost. Worse yet, a fraction of the scattered photons will still reach a detector and be registered in an erroneous position.

Combining PET and MR: solutions

The most straightforward way to create a PET/MR scanner is to adapt existing PET and MR machines to work in a tandem configuration, like PET/CT scanners do. The PET scanner can be inside the radiofrequency cage of the MR or in a separate room. An example of the former is Philips' Ingenuity TF system [12], whereas General Electric's Discovery PET/CT + MR represents the latter [13]. It goes without saying that physical distance is, by far, the best strategy to minimize all compatibility issues discussed in the previous section. This approach does, therefore, require minimal modifications of the existing scanners. The downside is the inability to perform truly simultaneous acquisitions and the long exam times caused by the sequential workflow.

When simultaneous acquisition is required, the most common solution is to build a PET detector ring capable of working within the bore of an MR scanner. The low budget approach to this, successfully adopted by many research groups in the past [14–24], is to build a removable PET insert to be used in a conventional MR scanner. An obvious limitation is the narrowing of the scanner bore due to the presence of the insert, restricting these systems to small animal studies and human brain scans.

Enabling simultaneous acquisition for whole-body studies requires some serious redesign of both subsystems. First and foremost is the need to find a space for the PET detectors within the MR. Both currently available integrated PET/MR scanners (Siemen's Biograph mMR [25] and General Electric's Signa PET/MR [26]) achieve this by basing their designs on a wide-bore MR scanner. Keeping the main coil and gradients of the wide-bore system and replacing the innermost radiofrequency coil with a narrow-bore version, a gap of approximately 10 cm is made available for the PET detector ring (Fig. 3).

First and foremost for this solution to work out, an alternative must be found for the PMTs in the PET detectors. Not only they are bulky, but also they just do not work within the magnetic field, which deflects the path of the electrons created by the photoelectric effect. Solid-state photodetector devices have been developed as an alternative to PMTs. Two such technologies are

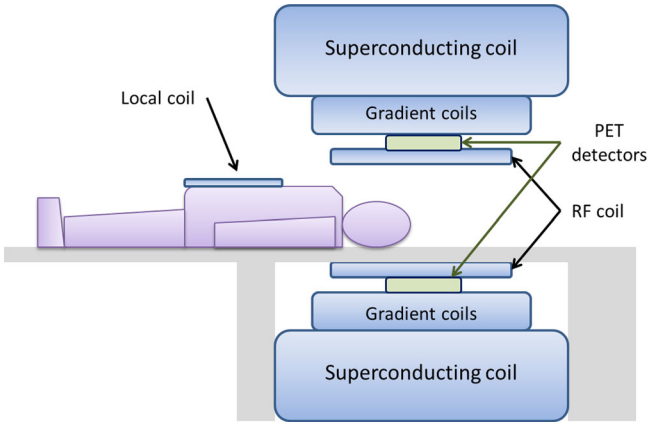

Fig. 3. Schematic representation (sagittal view) of an integrated PET/MR scanner. The superconducting coil and gradient coils of a wide-bore system are combined with the radiofrequency coil of a narrow-bore system, leaving a gap of a few centimeters where an MR-compatible detector ring can be installed.

currently in use: avalanche photodiodes (APD), used by the Biograph mMR, and silicon photomultipliers (SiPM), used by the Signa PET/MR. The former are a more mature technology, the latter being a more recent improvement offering, among other, good enough timing performance to achieve ToF-PET imaging.

One important drawback of these new photodetectors is their extreme sensitiveness to temperature changes. Indeed, temperature variations as low as one degree can have a measurable impact on their photon detection efficiency. Being confined in a narrow space and constantly bombarded with electromagnetic energy does, of course, not help. This calls for dedicated cooling by means of a constant flow of water (Signa PET/MR) or air (Biograph mMR), regulated by on-board temperature sensors.

Integrating the PET detectors behind the radiofrequency coil has the advantage of reducing the interference due to the MR excitation pulses. Still, radiofrequency shielding is required around the PET detectors and cables to minimize cross-talk. There are several constraints to be considered when designing this shielding: Will the chosen material cause non-uniformities in the magnetic field? Will eddy currents appear on the shield surface? Will heat build up on it? Will the portion of the shield in front of the PET detectors cause too much attenuation? An acceptable tradeoff can be achieved using conductor mesh layers, strategically cut to minimize the induction of eddy currents, as well as composite materials with tailored magnetic susceptibility, electrical and thermal conductivity (e.g., coated ceramics and polymer composites).

Last, but by no means least, is the issue of photon attenuation. Not only must all hardware placed in the field of view be redesigned to minimize attenuation, but also removing unnecessary material and relocating denser structures away from the patient. It is also of capital importance to know where the attenuating elements are located within the scanner. And this includes the patient himself.

The use of CT for attenuation correction in PET/CT is well established. CT images provide a measure of X-ray attenuation, both of patient tissue and hardware, which can be readily adapted for attenuation correction purposes. MR images, however, are based on different chemical properties of the tissue, not directly related to attenuation. Segmentation-based and atlas-based methods have been proposed to address this issue, and a recent review can be found in [27].

Both commercial simultaneous systems rely on the segmentation of MR sequences into four tissue classes (air, lungs, adipose, and soft tissue). These have certain limitations, such as: truncation of the attenuation maps; not correctly accounting for bone tissue; poor representation of the lung parenchyma; not accounting for inter-individual variability in attenuation coefficients; sensitivity to the presence of metallic implants. These issues are, however, the object of active research and several solutions have been proposed in the literature. We will discuss briefly the first two issues, for which specific solutions are already implemented in commercial simultaneous PET/MR systems.

The truncation issue is caused by the MR field of view being unable to encompass the entire patient breath. This entails that MR-based attenuation correction methods will miss some necessary information, usually the patient shoulders and arms, leading to bias in the PET images. To prevent this, the patient outline can be extracted from uncorrected ToF-PET images (as the Signa PET/MR does [28]) or an iterative approach can be used to infer the missing information from the PET emission data (as the Biograph mMR does [29]).

Bone tissue is another limitation of MR-based attenuation correction, due to the difficulty of distinguishing it from air with standard MR sequences. Ignoring bone attenuation has been shown to cause unacceptable bias in brain imaging [30], as well as for body features in the proximity of large bone structures [31, 32]. The use of atlas information [28] and ultrashort echo time MR sequences [33] have been proposed to address this issue.

Performance assessment

There are abundant publications concerning the performance of PET/MR systems, real or simulated, and how different aspects of their integration affect the final image quality and quantitation [25, 26]. And yet, there are few differences between evaluating the performance of a PET/MR system and evaluating the performance of standalone PET and MR scanners. We provide here a few tips concerning the most relevant performance parameters and how to interpret them.

Most of the MR hardware remains unchanged in hybrid PET/MR systems, making its performance pretty straightforward to evaluate. As a matter of fact, standard clinical sequences should be qualitatively indistinguishable from what could be expected from a standalone scanner. At least from an equivalent, wide-bore system. That said, the now narrow-bore transmit/receive coil will behave differently than its wide-bore counterpart would, and therefore so will the transmit gain settings. Also, some of the local coils may have been redesigned, leading to different (but not necessarily worse) sensitivity patterns.

Some parameters that may reflect the impact of the PET detectors on the MR are: The homogeneity of the static (B0) field; the receive-only spectrum; and the long-term stability. It goes without saying that these parameters should be considered both when the PET detectors are offline and when they are active.

Static field homogeneity maps should show deviations around 0.1 parts per million (root mean square) in a centered 20 cm sphere, and steadily increase to 1–2 parts per million in a 40 cm sphere. As a reference, 1 part per million (ppm) is equivalent to 0.0001%.

The receive spectrum shows how much signal is being received throughout the MR operating band. With the scanner in receive-only mode, the spectrum should be flat. Spikes in the spectrum would either mean that the Faraday cage is not doing its job properly and we are picking up radio signals from the outside, or that the PET detectors are insufficiently shielded.

Stability measurements are common for applications such as functional MRI. They reflect the ability of the system to cope with the effects of long-term acquisitions, such as heat buildup. Root mean square stability values below 0.1% and absolute drift below 1% should be expected.

Concerning PET performance, the evaluation requires a bit more caution, as the redesign of the detectors for their integration in the MR bore had some significant, and in some cases unexpected, consequences. In any case, the widespread NEMA [34] and EARL [35] tests commonly used for PET performance evaluation can easily be adapted to PET/MR (with the use of a template for attenuation correction of the image quality phantom). Some parameters that may reflect the impact of MR on PET are: sensitivity; count rate curves; spatial resolution; and image quality. These parameters should be considered with the MR scanner offline, but also when different MR sequences are being acquired (e.g., a radiofrequency-intensive sequence and a gradient-intensive sequence), as they may alter the PET detectors' performance.

PET sensitivity is one of the most misleading parameters in PET/MR. Due to the space constraints imposed by MR, integrated PET rings are longer and narrower than their standalone counterparts. Which is actually a good thing, as more photons will be captured (the ideal PET scanner being one where the patient is covered head to feet in detectors). This is the main reason why the sensitivity of PET/MR scanners is spectacularly better than that of equivalent standalone systems. But there are several caveats: firstly, the scanner will reach the saturation for lower activities (not necessarily a problem if the injected dose is reduced accordingly). Secondly, the number of scattered and random events detected will increase more than the true events do. Thirdly, the increase of sensitivity derived from a larger axial coverage is only relevant for certain examinations (i.e., extending the field of view to include the neck will not make brain images look any better).

For the reasons listed above, it is important to take a long look at the scanner count rate curves, particularly the noise equivalent count rate (NECR) and scatter fraction. The peak NECR value is a good reference of the raw data quality that can be acquired by a system, but it is important to contemplate at what activity level is that peak reached and adjust clinical protocols accordingly (e.g., the Signa PET/MR has optimal NECR at 18 kBq/mL, compared to the 29 kBq/mL of the Discovery 690 PET/CT).

Spatial resolution is not a particularly relevant parameter in PET/MR systems, behaving essentially like it does in standalone systems. This might come as a surprise to those familiar with the history of PET/MR. Indeed, the first attempts at an hybrid scanner were motivated by the assumption that the magnetic field would reduce the distance traveled by positrons before annihilating, thus improving the spatial resolution of PET. While this is true (for transaxial resolution only) the resolution gain has been shown to be negligible given the field strengths and positron energies commonly found in clinical practice. The effect may still be noticeable, however, for certain tracers and in low-density tissue regions [36].

Finally, image quality measurements can provide a good idea of the performance of a system in terms of small lesion detectability. But, as already mentioned, this measurement requires the use of an attenuation map for PET reconstruction. Unfortunately, current MR-based attenuation correction algorithms are optimized for human imaging and will not work properly on phantoms. Scanners may include a dedicated setting for phantom scanning, but it will not be representative of how attenuation correction performs on humans.

For this reason, it is critical to perform qualitative inspections of the attenuation maps generated by a PET/MR system, preferably comparing them with a CT-based attenuation map of the same subject. The number of tissue classes, accuracy of truncation completion, treatment of bone and air cavities, inclusion of hardware elements, and impact of respiratory motion are some of the aspects that should be evaluated. Robustness and

repeatability, rather than accuracy, should be sought after.

Conclusions

Hybrid positron emission and magnetic resonance scanners are a new and promising imaging modality, combining two of the most versatile technologies currently available. Bridging these two worlds, however, can make PET/MR scanners appear somewhat intimidating, reserved for that elite minority of experts in both Nuclear Medicine and Radiology. In this work, we have tried to provide the basic knowledge required by any physician to understand, evaluate, and make use of state-of-the-art clinical PET/MR systems.

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